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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,138	05/05/2006	Tobias Wunberg	Le A 36 437	8469

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EXAMINER	
TRUONG, TAMTHOM NGO	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,138	WUNBERG ET AL.	
	Examiner	Art Unit	
	TAMTHOM N. TRUONG	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006 (Prelim. Amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6 and 9-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment of 5-5-06 has been entered and acknowledged. Claims 5, 7 and 8 are cancelled. Claims 1-4, 6 and 9-17 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-4, 6 and 9-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

   a. Claims 1-3 and dependent claims recite the term "solvates" which is not defined in the specification in terms of what appropriate solvents are and in what proportions. Thus, it is indefinite as to what constitutes a solvate.

   b. Claim 4 recites the term "preferably" which has indefinite metes and bounds because it is not clear if the limitation following said term is part of the claim.

2. **Essential Step Omitted:** Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is the step involving the reaction including HCL which is critical or essential to the practice of the

invention, but not included in the claim(s) which makes claim 4 incomplete. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim 4 recites a process of making formula (I) by reacting formula (II) (an ester of $-C(=O)-OR^{10}$) with a base which would not yield an acid side chain at the 4-position of formula (I) (i.e., -C(=O)-OH). Thus, claim 4 is missing an essential step.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 1-4, 6 and 9-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula (I), does not reasonably provide enablement for "solvates" of said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;
(2) The amount of direction or guidance presented;
(3) The state of the prior art;
(4) The relative skill of those in the art;
(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 1-3 recite the limitation of "solvates" of compounds represented by formula (I). The term "solvates" covers various forms of the same compound at different proportions of solvents. Thus, the scope of "solvates" of said claims and claims dependent thereon is unduly broad.

The amount of direction or guidance presented: The specification does not describe "solvates" or provide guidance on what proportion of solvents to use for obtaining a "solvate". Thus, the specification fails to provide sufficient enablement for making a "solvate" of the claimed compounds.

The state of the prior art: Although it is not unusual to expect a "solvate" of a compound, the process for selecting a solvent to make a solvate is not standard for all drugs since not all solvents can form solvates with all compounds. For the claimed compound, there is no reference teaching any possible solvate. Furthermore, the teaching of **Vippagunta** flatly states on page 18, section 3.4 the following:

> "Predicting the formation of solvates or hydrates of a compound…is complex and difficult."

Thus, the state of the prior art does not support the broad scopes of "solvates" in the above claims.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select a "solvate" for each compound from the large Markush group of formula (I). Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and active metabolites for each "solvate". Given a large Markush group of formula(I), such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a "solvate" is quite unpredictable because it is not possible to predict whether solid solutions will form and at what stoichiometry proportion (i.e, one, two, or half a molecule of solvent added per molecule of host) – see the following excerpt of **Vippagunta et. al.** :

> Each solid compound responds uniquely to the possible formation of solvates…and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent;…There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of …solvates.

(*Vippagunta et. al., Crystalline solids, Advanced Drug Delivery Review, 48(2001) 3-26)*

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make the hundreds of thousands of compounds and "solvates" of compounds represented by formula (I) recited in the above claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

Tamthom N. Truong
Patent Examiner, Art Unit 1624

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3-24-09